AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claims 1-21 (Canceled as prosecuted in a previous application)

Claim 22. (Currently Amended): A method of inserting a heterologous gene coding sequence into an endogenous gene in a mouse embryonic stem cell genome and expressing said heterologous gene coding sequence, comprising the step of transforming the mouse embryonic stem cell with a random gene trap vector comprising a DNA construct, wherein the ~~DNA construct (k)~~ heterologous gene coding sequence lacks a promoter, and (ii) comprises the sequence:

~~5' A P B Q O 3'~~

~~in which~~

~~P is an internal ribosome entry site (IRES)~~

~~Q is the heterologous gene sequence, and~~

~~A, B and C are, separately, optional linker sequences;~~

~~wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q~~

5' X-A-P-B-Q-C-Y 3'

in which

~~comprises a splice acceptor sequence;~~

~~Y comprises a polyadenylation signal;~~

X and Y	are separately, DNA sequences substantially homologous with a host gene locus;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene sequence, including a translation start codon; and
A, B, and C	are, separately, optional linker sequence[s];

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q.

Claim 23. (Original): A method according to Claim 22 where the heterologous gene coding sequence is randomly inserted into an endogenous gene so that transcription of the heterologous gene coding sequence is directed by the host regulatory elements of the endogenous gene.

Claim 24. (Original): A method according to Claim 22 in which the splice acceptor permits functional integration of the heterologous gene coding sequence into an intron sequence.

Claim 25. (Canceled)

Claim 26. (Original): A method according to Claim 22 further comprising the step of identifying cells expressing the heterologous gene coding sequence.

Claim 27. (Currently Amended): A method according to Claim 26 wherein the ~~heterologous gene coding sequence~~ construct also ~~codes for~~ comprises a gene encoding a selectable marker and the method comprises selecting cells that express the selectable marker.

Claim 28. (Previously Amended) A mouse embryonic stem cell comprising a heterologous gene code sequence inserted by the method of Claim 22.

Claim 29. (Previously Amended) A descendant of the mouse embryonic stem cell according to Claim 28, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 30. (Withdrawn): An animal comprising a heterologous gene coding sequence inserted by the method of Claim 22.

Claim 31. (Withdrawn): A descendant of an animal according to Claim 30, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 32. (Currently Amended): A DNA construct for randomly inserting a heterologous gene sequence into a mouse cell genome, said ~~construct~~ heterologous gene sequence lacking a promoter and comprising the sequence:

~~5' A P B Q C 3'~~

~~in which~~

~~P is an internal ribosome entry site (IRES);~~

~~Q is a heterologous gene sequence; and~~

~~A, B and C are, separately, optional linker sequences;~~

~~wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q~~

5' X-A-P-B-Q-C-Y 3'

in which

	~~comprises a splice acceptor sequence;~~
~~Y~~	~~comprises a polyadenylation signal;~~
X and Y	are separately, DNA sequences substantially homologous with a host gene locus;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene sequence, including a translation start codon; and
A, B and C	are, separately, optional linker sequence[s];

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q.

Claim 33. (Original): A DNA construct according to Claim 32 in which the splice acceptor permits functional integration of the heterologous gene into an intron sequence.

Claim 34. (Currently Amended): A DNA construct according to Claim 32 in which the ~~heterologous gene sequence additionally codes for~~ construct also comprises a gene encoding a selectable marker to facilitate selection of mouse cells containing a heterologous gene that has been inserted into an endogenous gene.

Claim 35 (Withdrawn): A method of inserting a heterologous gene coding sequence into an endogenous gene in a eukaryotic cellular host cell genome and expressing said heterologous gene coding sequence, comprising the step of transforming the host cell with a random gene trap vector comprising a DNA construct, wherein the heterologous gene coding sequence (1) lacks a promoter, and (2) comprises the sequence:

5' X-A-P-B-Q-C-Y-Z 3'

in which

X	comprises a splice acceptor;
Y	comprises a polyadenylation signal;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene sequence;
A, B, and C	are, separately, optional linker sequences; and
Z	is a selectable marker cassette optionally adapted for recombinatorial

deletion following introduction of an X-A-P-B-Q-C-Y-Z construct in a gene which is not expressed in ES cells.

Claim 36 (Withdrawn): A method according to Claim 35 wherein the heterologous gene coding sequence is inserted into an endogenous gene so that transcription of the heterologous gene coding sequence is directed by the host regulatory elements of the endogenous gene.

Claim 37 (Withdrawn): A method according to Claim 35 in which the splice acceptor permits functional integration of the heterologous gene coding sequence into an intron sequence.

Claim 38 (Withdrawn): A method according to Claim 35 wherein the heterologous gene coding sequence is expressed in an animal cell.

Claim 39 (Withdrawn): A method according to Claim 35 further comprising the step of identifying cells expressing the heterologous gene coding sequence.

Claim 40 (Withdrawn): A method according to Claim 36 wherein the heterologous gene coding sequence also codes for a selectable marker, such as antibiotic resistance, and the method comprises selecting cells that express the selectable marker.

Claim 41. (Currently Amended): A method according to Claim 22 wherein the ~~heterologous gene coding sequence~~ construct also ~~codes for~~ comprises a gene encoding antibiotic resistance, and the method comprises selecting cells that express the antibiotic resistance.

Claim 42. (Currently Amended): A DNA construct according to Claim 32 wherein the ~~heterologous gene sequence~~ construct additionally ~~codes for~~ comprises a gene encoding antibiotic resistance.

Claims 43-46 (Canceled)

Claim 47. (New): A method of inserting a heterologous gene coding sequence into an endogenous gene in a mouse embryonic stem cell genome and expressing said heterologous gene coding sequence, comprising the step of transforming the mouse embryonic stem cell with a random gene trap vector comprising a DNA construct, wherein the heterologous gene coding sequence lacks a promoter, and comprises the sequence:

5' A-P-B-Q-C 3'

in which

P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene sequence, and
A, B and C	are, separately, optional linker sequences;

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q.

Claim 48. (New): A method according to Claim 47 where the heterologous gene coding sequence is randomly inserted into an endogenous gene so that transcription of the

heterologous gene coding sequence is directed by the host regulatory elements of the endogenous gene.

Claim 49. (New): A method according to Claim 47 in which the splice acceptor permits functional integration of the heterologous gene coding sequence into an intron sequence.

Claim 50. (New): A method according to Claim 47 further comprising the step of identifying cells expressing the heterologous gene coding sequence.

Claim 51. (New): A method according to claim 50 wherein the construct also comprises a gene encoding a selectable marker and the method comprises selecting cells that express the selectable marker.

Claim 52. (New): A mouse embryonic stem cell comprising a heterologous gene coding sequence inserted by the method of Claim 47.

Claim 53. (New): A descendant of the mouse embryonic stem cell according to Claim 52, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 54. (New): A mouse comprising a cell according to Claim 53.

Claim 55. (New): A descendant of a mouse according to Claim 54, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 56. (New): A DNA construct comprising the sequence:

5' A-P-B-Q-C 3'

in which

P	is an internal ribosome entry site (IRES);
Q	is a heterologous gene sequence; and
A, B and C	are, separately, optional linker sequences;

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of Q.

Claim 57. (New): A DNA construct according to Claim 56 in which the splice acceptor permits functional integration of the heterologous gene into an intron sequence.

Claim 58. (New): A DNA construct according to Claim 56 in which the construct also comprises a gene encoding a selectable marker to facilitate selection of cells containing a heterologous gene that has been inserted into an endogenous gene.

Claim 59. (New): A method according to Claim 47, wherein the construct also comprises a gene encoding antibiotic resistance, and the method comprises selecting cells that express the antibiotic resistance.

Claim 60. (New): A DNA construct according to Claim 56, wherein the construct additionally comprises a gene encoding antibiotic resistance.

Claim 61. (New): A mouse comprising a heterologous gene coding sequence inserted by the method of claim 22.

Claim 62. (New): A descendant of the mouse according to Claim 61, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 63. (New): A cell comprising a heterologous gene coding sequence inserted according to the method of Claim 56.

Claim 64. (New): A descendant of the cell according to Claim 63, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 65. (New): A mouse comprising a heterologous gene coding sequence inserted according to the method of Claim 56.

Claim 66. (New): A descendant of the mouse according to Claim 65, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 67. (New): A cell comprising an inserted heterologous gene coding sequence inserted into a target endogenous gene in a eukaryotic cellular host cell genome by transforming the host cell with a vector comprising a DNA construct, wherein the DNA construct comprises the elements:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are substantially homologous with separate sequences from the target endogenous gene and are of sufficient length to undergo homologous recombination with the host cell genome so as to insert the A-P-B-Q-C elements into the host cell genome;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene coding sequence; and
A, B, and C	are, separately, linker sequence or a covalent bond.

Claim 68. (New): A descendant of the cell of Claim 67, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 69. (New): A mouse comprising an inserted heterologous gene coding sequence inserted into a target endogenous gene in a eukaryotic cellular host cell genome by transforming the host cell with a vector comprising a DNA construct, wherein the DNA construct comprises the elements:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are substantially homologouse with separate sequences from the target endogenous gene and are of sufficient length to undergo homologous recombination with the host cell genome so as to insert the A-P-B-Q-C elements in to the host cell genome;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene coding sequence; and
A, B, and C	are, separately, linker sequence or a covalent bond.

Claim 70. (New): A descendant of the mouse of Claim 69, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claim 71. (New): A cell according to Claim 67, wherein the construct also comprises a gene encoding a selectable marker.

Claim 72. (New): A mouse according to Claim 69, wherein the construct also comprises a gene encoding a selectable marker.

Claim 73. (New): A DNA construct for inserting a heterologous gene coding sequence into a target endogenous gene in a eukaryotic cellular host cell genome, wherein the construct comprises the elements:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are substantially homologous with separate sequences from the target endogenous gene and are of sufficient length to undergo homologous recombination with the host cell genome so as to insert the A-P-B-Q-C elements into the host cell genome;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene coding sequence; and
A, B, and C	are, separately, linker sequence or a covalent bond.

Claim 74. (New): The DNA construct according to Claim 73, wherein the construct also comprises a gene encoding a selectable marker.